

In the claims, please amend as follows:

1. (Withdrawn) Use of a multifunctional steroid compound comprising
  - i) a steroid component,
  - ii) at least one SOD mimic component, and optionally
  - iii) at least one NO donor componentin the preparation of a medicament.
2. (Withdrawn) Use of a multifunctional steroid compound according to claim 1, comprising
  - i) a steroid component,
  - ii) at least one SOD mimic component linked to said steroid component, and
  - iii) at least one NO donor component linked to said steroid component.
3. (Withdrawn) Use according to claim 1, wherein said steroid comprises cyclopenta[a]phenantrene, said SOD mimic component comprises an antioxidant reacting with superoxide, and said NO donor comprises a group capable of providing nitric oxide in a form selected from uncharged, free radical, and charged.
4. (Withdrawn) Use according to claim 1, wherein said SOD mimic component comprises a substituted N-oxide free radical.
5. (Withdrawn) Use according to claim 4, wherein the N-atom of said N-oxide is a member of 3 to 7 membered heterocyclic ring.
6. (Withdrawn) Use according to claim 2, wherein said NO donor component comprises a group selected from  $\text{—ONO}_2$ ,  $\text{—ONO}$ ,  $\text{—SNO}$ , and  $\text{—NONOate}$ .
7. (Withdrawn) Use of a multifunctional steroid compound according to claim 1 in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of disorders associated with oxidative stress and free radical injury,

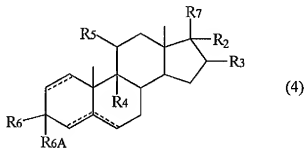
disorders in which treatment with steroids or their analogs is indicated, and disorders in which treatment with a smooth muscle relaxant is indicated.

8. (Withdrawn) Use of a multifunctional steroid compound according to claim 1 in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of respiratory, pulmonary, cardiovascular, inflammatory, and autoimmune disorders.

9. (Withdrawn) Use of a multifunctional steroid compound according to claim 1 in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, Chronic Obstructive Pulmonary Diseases (COPDs), bronchial hyperreactivity, respiratory distress syndrome or Chronic Obstructive Airway Disease (COADs), allergic conditions, arthritis, autoimmune hematologic disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-versus-host disease, multiple sclerosis, Alzheimer diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, disorders related to learning, disorders related to olfaction, disorders related to nociception, cerebral edema, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions, drug and disease-induced neuropathies and nephropathies, pathological uterine contractions, sinus tachycardia, ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders, hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholesterolemia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion tissue injury, chemotaxis and phagocytic impairment in immunological disorders, aging-mediated changes, cerebrovascular

diseases, thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection.

10. (Withdrawn) Use of a multifunctional steroid compound according to claim 1, wherein said steroid compound has formula (4)



optical isomers thereof, salts thereof, and solvates thereof;

wherein        is a single or double bond, with the proviso that two double bonds are not adjacent;

R<sup>2</sup> is —H, —ONO, —ONO<sub>2</sub>, —SNO, —OH, —CH<sub>3</sub>, —NONOate, —OC(O)R<sup>8</sup> wherein R<sup>8</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl or 5- or 6-member heteroaryl, or R<sup>2</sup> and R<sup>7</sup> together form a substituted N-oxide free radical;

R<sup>3</sup> is —H, —OH, or —CH<sub>3</sub>, or R<sup>2</sup> and R<sup>3</sup> together form a heterocyclic ring;

R<sup>4</sup> is —H or halogen;

R<sup>5</sup> is —H, =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate or a substituted N-oxide free radical;

R<sup>6</sup> is =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate, and

R<sup>6A</sup>, if present, is —H, or R<sup>6</sup> and R<sup>6A</sup> together form a substituted N-oxide free radical;

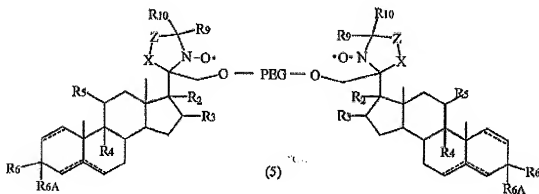
R<sup>7</sup> is —H, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate, or a substituted N-oxide free radical wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring, which ring is optionally substituted by —OCOCH<sub>2</sub>-PEG wherein said PEG may be optionally coupled to another steroid compound, and which ring is further optionally substituted by or one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups which may be further independently substituted by a group selected from

an NO donor component,  $\text{—SR}^{11}$ ,  $\text{—halogen}$ , and  $\text{—OC(O)R}^{13}$  wherein  $\text{R}^{11}$  is  $\text{C}_1\text{—C}_5$  alkyl and wherein  $\text{R}^{13}$  is  $\text{C}_1\text{—C}_5$  alkyl or 5- or 6-member heteroaryl, or  $\text{R}^2$  and  $\text{R}^7$  together form a substituted N-oxide free radical; and

wherein NO donor is a group comprising one of  $\text{—ONO}_2$ ,  $\text{—ONO}$ ,  $\text{—SNO}$ , and  $\text{—NONOate}$ , and

wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected  $\text{C}_1\text{—C}_5$  alkyl groups which may be further independently substituted by an NO donor component.

11. (Withdrawn) Use according to claim 10, wherein said steroid compound has formula (5)



wherein the  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ , and  $\text{R}^{6A}$  are as defined in claim 10;

$\text{R}^9$  and  $\text{R}^{10}$  are independently, linear or branched  $\text{C}_1\text{—C}_5$  alkyl groups, or substituted linear or branched  $\text{C}_1\text{—C}_5$  alkyl groups wherein the alkyl group is independently substituted by an NO donor or  $\text{—OC(O)R}^{14}$ , wherein  $\text{R}^{14}$  is  $\text{C}_1\text{—C}_5$  alkyl, or 5- or 6-member heteroaryl;

$\text{X}$  is  $\text{—CH}_2\text{—}$ ,  $\text{—O—}$  or  $\text{—S—}$ ;

$\text{Z}$  is  $\text{—CH}_2\text{—}$  or  $\text{—CH}_2\text{—CH}_2\text{—}$ ;

and PEG is a polyethylene glycol of a molecular weight from about 100 to about 4000.

12. (Withdrawn) Use according to claim 10, wherein said steroid compound has a formula selected from Ia to Id (below) wherein

$R^2$  is —H, —ONO, —ONO<sub>2</sub>, —SNO, —OH, —CH<sub>3</sub>, —NONOate, or —OC(O)R<sup>8</sup>, wherein R<sup>8</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, or 5- or 6-member heteroaryl;

$R^3$  is —H, —OH, or —CH<sub>3</sub>, or  $R^2$  and  $R^3$  together form a heterocyclic ring;

$R^4$  is —H or halogen;

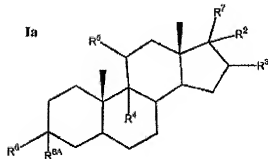
$R^5$  is —H, =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups;

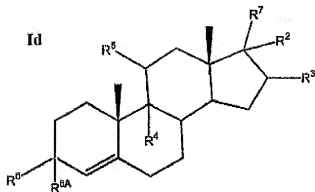
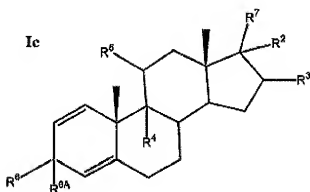
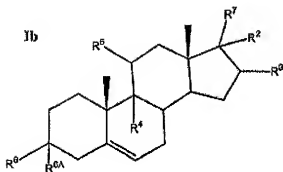
$R^6$  is =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate, and

$R^{6A}$ , if present, is —H, or  $R^6$  and  $R^{6A}$  together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide

free radical is within a 5- or 6- member ring substituted by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups which may be may be further independently substituted by an NO donor component;

$R^7$  is —H, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate, or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring optionally substituted by —OCOCH<sub>2</sub>-PEG or one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups which may be further independently substituted by an NO donor component, —SR<sup>11</sup>—halogen, or —OC(O)R<sup>13</sup>, wherein R<sup>11</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, and wherein





$R^{13}$  is  $C_1$ - $C_5$  alkyl, or 5- or 6-member heteroaryl, or  $R^2$  and  $R^7$  together form a substituted N-oxide free radical; and

NO donor is a group comprising one of  $—ONO_2$ ,  $—ONO$ ,  $—SNO$ , and  $—NONOate$ ;

wherein at least one of  $R^2$ ,  $R^5$ ,  $R^6$ , or  $R^7$  comprises an NO donor; and

wherein at least one of  $R^5$ ,  $R^6$ , or  $R^7$  comprises a substituted N-oxide free radical.

13. (Withdrawn) Use according to claim 10, wherein said steroid compound has a formula selected from IIa to IIc (below) wherein

$R^2$  is —H, —ONO, —ONO<sub>2</sub>, —SNO, —OH, —CH<sub>3</sub>, —NONOate, or —OC(O)R<sup>8</sup>, wherein R<sup>8</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, or 5- or 6-member heteroaryl;

R<sup>3</sup> is —H, —OH, or —CH<sub>3</sub>, or R<sup>2</sup> and R<sup>3</sup> together form a heterocyclic ring;

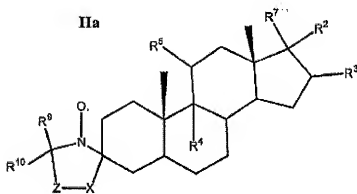
R<sup>4</sup> is —H or halogen;

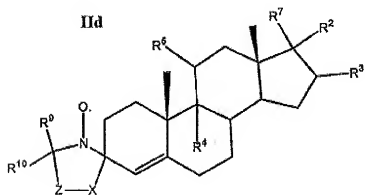
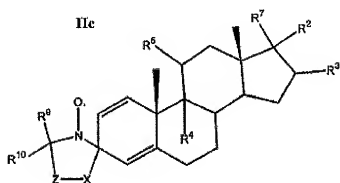
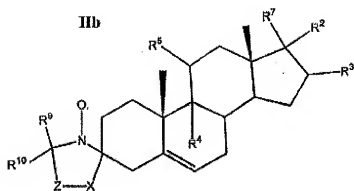
R<sup>5</sup> is —H, =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups;

R<sup>7</sup> is —H, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate, or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by

—OCOCH<sub>2</sub>-PEG or by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups, wherein said alkyl group may be further independently substituted by an NO donor, —SR<sup>11</sup>, —halogen, or —OC(O)R<sup>13</sup>, wherein R<sup>11</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, and wherein R<sup>13</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl or 5- or 6-member heteroaryl;

R<sup>9</sup> and R<sup>10</sup> are independently, linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl groups or substituted linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl groups wherein said alkyl group may be substituted by an NO donor or —OC(O)R<sup>14</sup>, wherein R<sup>14</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl or 5- or 6-member heteroaryl;





X is  $\text{---CH}_2\text{---}$ ,  $\text{---O---}$  or  $\text{---S---}$ ;

Z is  $\text{---CH}_2\text{---}$  or  $\text{---CH}_2\text{---CH}_2\text{---}$ ;

NO donor is a group comprising one of  $\text{---ONO}_2$ ,  $\text{---ONO}$ ,  $\text{---SNO}$ , and  $\text{---NONOate}$ ; and

wherein at least one of  $\text{R}^2$ ,  $\text{R}^5$ ,  $\text{R}^7$ ,  $\text{R}^9$  or  $\text{R}^{10}$  comprises an NO donor.



14. (Withdrawn) Use according to claim 10, wherein said steroid compound has a formula selected from IIIa to IIId (below) wherein

R<sup>1</sup> is —H, —OH, —OCOCH<sub>2</sub>-PEG, linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl, linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl substituted by an NO donor, —SR<sup>11</sup>, —halogen, or —OC(O)R<sup>15</sup>, wherein R<sup>11</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, wherein R<sup>15</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl;

R<sup>2</sup> is —H, —ONO, —ONO<sub>2</sub>, —SNO, —OH, —CH<sub>3</sub>, —NONOate, or —OC(O)R<sup>8</sup>, wherein R<sup>8</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, or 5- or 6-member heteroaryl;

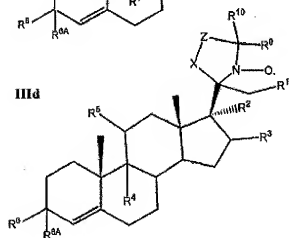
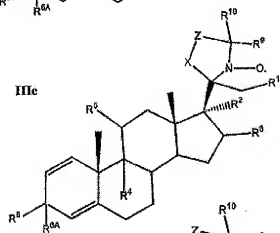
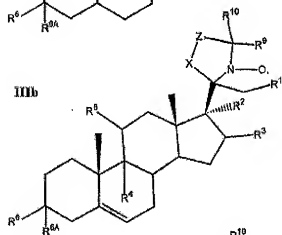
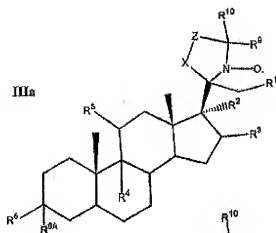
R<sup>3</sup> is —H, —OH, or —CH<sub>3</sub>, or R<sup>2</sup> and R<sup>3</sup> together form a heterocyclic ring;

R<sup>4</sup> is —H or halogen;

R<sup>5</sup> is —H, =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups;

R<sup>6</sup> is =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate, and R<sup>6A</sup>, if present, is —H, or R<sup>6</sup> and R<sup>6A</sup> together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups, wherein said alkyl may be further substituted by an NO donor, or —OC(O)R<sup>12</sup>, wherein R<sup>12</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, or 5- or 6-member heteroaryl;

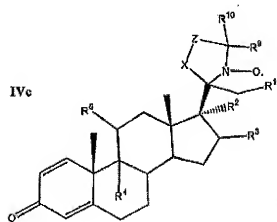
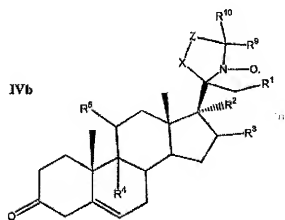
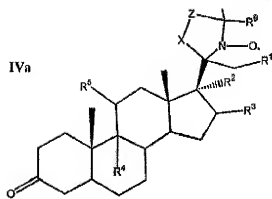
R<sup>9</sup> and R<sup>10</sup> are independently, linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl groups, or substituted linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl groups wherein said alkyl group is

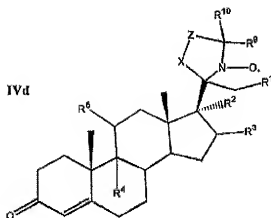


independently substituted by  $\text{---ONO}$ ,  $\text{---ONO}_2$ ,  $\text{---SNO}$ ,  $\text{---NONOate}$  or  $\text{---OC(O)R}^{14}$ , wherein  $\text{R}^{14}$  is  $\text{C}_1\text{---C}_5$  alkyl;  
 $\text{X}$  is  $\text{---CH}_2\text{---}$ ,  $\text{---O---}$  or  $\text{---S---}$ ;  
 $\text{Z}$  is  $\text{---CH}_2\text{---}$  or  $\text{---CH}_2\text{---CH}_2\text{---}$ ;  
 wherein an NO donor is a group comprising one of  $\text{---ONO}_2$ ,  $\text{---ONO}$ ,  $\text{---SNO}$ , and  $\text{---NONOate}$ ; and  
 wherein at least one of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^9$  or  $\text{R}^{10}$  comprises at least one NO donor.

15. (Withdrawn) Use according to claim 10, wherein said steroid compound has formula a formula selected from IVa to IVd (below) wherein

$\text{R}^1$  is  $\text{---H}$ ,  $\text{---OH}$ ,  $\text{---OCOCH}_2\text{---PEG}$ ; linear or branched  $\text{C}_1\text{---C}_5$  alkyl; linear or branched  $\text{C}_1\text{---C}_5$  alkyl substituted by an NO donor,  $\text{---SR}^{11}$ ,  $\text{---halogen}$ , or  $\text{---OC(O)R}^{15}$ , wherein  $\text{R}^{11}$  is  $\text{C}_1\text{---C}_5$  alkyl, and wherein  $\text{R}^{15}$  is  $\text{C}_1\text{---C}_5$  alkyl;  
 $\text{R}^2$  is  $\text{---H}$ ,  $\text{---ONO}$ ,  $\text{---ONO}_2$ ,  $\text{---SNO}$ ,  $\text{---OH}$ ,  $\text{---CH}_3$ ,  $\text{---NONOate}$ , or  $\text{---OC(O)R}^8$ , wherein  $\text{R}^8$  is  $\text{C}_1\text{---C}_5$  alkyl, or 5- or 6-member heteroaryl;  
 $\text{R}^3$  is  $\text{---H}$ ,  $\text{---OH}$ , or  $\text{---CH}_3$ , or  $\text{R}^2$  and  $\text{R}^3$  together form a heterocyclic ring;  
 $\text{R}^4$  is  $\text{---H}$  or halogen;  
 $\text{R}^5$  is  $\text{---H}$ ,  $\text{=O}$ ,  $\text{---ONO}$ ,  $\text{---ONO}_2$ ,  $\text{---SNO}$ ,  $\text{---NONOate}$  or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected  $\text{C}_1\text{---C}_5$  alkyl groups;  $\text{R}^9$  and  $\text{R}^{10}$  are independently, linear or branched  $\text{C}_1\text{---C}_5$  alkyl groups, or substituted linear or branched  $\text{C}_1\text{---C}_5$  alkyl groups wherein the said group is independently substituted by an NO donor or  $\text{---OC(O)R}^{14}$ , wherein  $\text{R}^{14}$  is  $\text{C}_1\text{---C}_5$  alkyl;  
 $\text{X}$  is  $\text{---CH}_2\text{---}$ ,  $\text{---O---}$  or  $\text{---S---}$ ;  
 $\text{Z}$  is  $\text{---CH}_2\text{---}$  or  $\text{---CH}_2\text{---CH}_2\text{---}$ ;





wherein an NO donor is a group comprising one of  $\text{—ONO}_2$ ,  $\text{—ONO}$ ,  $\text{—SNO}$ , and  $\text{—NONOate}$ ; and

wherein at least one of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^5$ ,  $\text{R}^9$  or  $\text{R}^{10}$  comprises at least one NO donor.

16. (Withdrawn) Use according to claim 10, wherein said steroid compound has a formula selected from Va to Vd (below) wherein

$\text{R}^3$  is  $\text{—H}$ ,  $\text{—OH}$ , or  $\text{—CH}_3$ ;

$\text{R}^4$  is  $\text{—H}$  or halogen;

$\text{R}^5$  is  $\text{—H}$ ,  $\text{=O}$ ,  $\text{—ONO}$ ,  $\text{—ONO}_2$ ,  $\text{—SNO}$ ,  $\text{—NONOate}$  or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected  $\text{C}_1\text{—C}_5$  alkyl groups;

$\text{R}^6$  is  $\text{=O}$ ,  $\text{—ONO}$ ,  $\text{—ONO}_2$ ,  $\text{—SNO}$ ,  $\text{—NONOate}$ ,

and  $\text{R}^{6A}$ , if present, is  $\text{—H}$ , or  $\text{R}^6$  and  $\text{R}^{6A}$  together form a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected  $\text{C}_1\text{—C}_5$  alkyl groups wherein said alkyl groups may be further substituted by an NO donor, or  $\text{—OC(O)R}^{12}$ , wherein  $\text{R}^{12}$  is  $\text{C}_1\text{—C}_5$  alkyl, or 5- or 6-member heteroaryl;

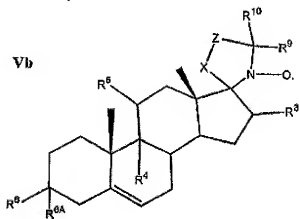
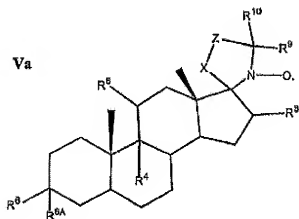
$\text{R}^9$  and  $\text{R}^{10}$  are independently, linear or branched  $\text{C}_1\text{—C}_5$  alkyl groups, or substituted linear or branched  $\text{C}_1\text{—C}_5$  alkyl groups wherein the alkyl group is independently substituted by an NO donor or  $\text{—OC(O)R}^{14}$ , wherein  $\text{R}^{14}$  is  $\text{C}_1\text{—C}_5$  alkyl, or 5- or 6-member heteroaryl;

X is  $-\text{CH}_2-$ ,  $-\text{O}-$  or  $-\text{S}-$ ;

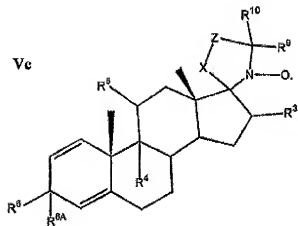
Z is  $-\text{CH}_2-$  or  $-\text{CH}_2-\text{CH}_2-$ ;

wherein an NO donor is a group comprising one of  $-\text{ONO}_2$ ,  $-\text{ONO}$ ,  $-\text{SNO}$ , and  $-\text{NONOate}$ ; and

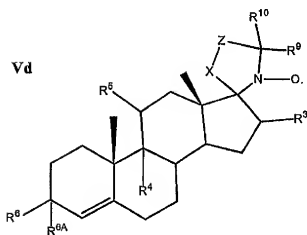
wherein at least one of  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^9$  or  $\text{R}^{10}$  comprises an NO donor.



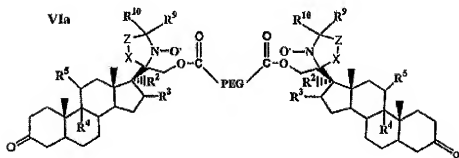
Vc

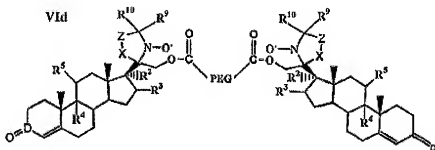
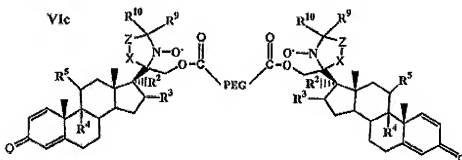
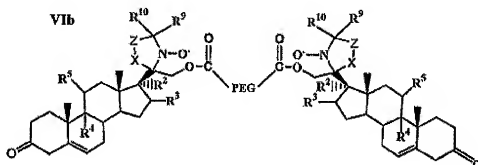


Vd



Vla





17. (Withdrawn) Use according to claim 11, wherein said steroid compound has formula a selected from VIa to VIId (above) wherein

$R^2$  is  $-H$ ,  $-ONO$ ,  $-ONO_2$ ,  $-SNO$ ,  $-OH$ ,  $-CH_3$ ,  $-NONOate$ , or  $-OC(O)R^8$ , wherein  $R^8$  is  $C_1$ - $C_5$  alkyl, or 5- or 6-member heteroaryl;

$R^3$  is  $-H$ ,  $-OH$ , or  $-CH_3$ , or  $R^2$  and  $R^3$  together form a heterocyclic ring;



R<sup>4</sup> is —H or halogen;

R<sup>5</sup> is —H, =O, —ONO, —ONO<sub>2</sub>, —SNO, —NONOate or a substituted N-oxide free radical, wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected C<sub>1</sub>-C<sub>5</sub> alkyl groups;

R<sup>9</sup> and R<sup>10</sup> are independently, linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl groups, or substituted linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl groups wherein the alkyl group is independently substituted by an NO donor or —OC(O)R<sup>14</sup>, wherein R<sup>14</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl, or 5- or 6-member heteroaryl;

X is —CH<sub>2</sub>—, —O— or —S—;

Z is —CH<sub>2</sub>— or —CH<sub>2</sub>-CH<sub>2</sub>—;

wherein an NO donor is a group comprising one of —ONO<sub>2</sub>, —ONO, —SNO, and —NONOate; and

wherein at least one of R<sup>2</sup>, R<sup>5</sup>, R<sup>9</sup> or R<sup>10</sup> comprises at least one NO donor.

18. (Withdrawn) Use according to claim 10 wherein R<sup>3</sup> is —H, —OH, or —CH<sub>3</sub>; R<sup>4</sup> is —H, F, or Cl; and R<sup>5</sup> is —H, =O, or —ONO<sub>2</sub>.

19. (Withdrawn) Use according to claim 11 wherein X is —CH<sub>2</sub>— or —O—, Z is —CH<sub>2</sub>—, and R<sup>9</sup> and R<sup>10</sup> are independently methyl or ethyl.

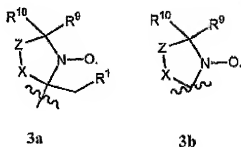
20. (Withdrawn) Use according to claim 10 wherein R<sup>2</sup> is —H or —ONO<sub>2</sub>.

21. (Withdrawn) Use according to claim 10 wherein R<sup>6</sup> is =O, —ONO<sub>2</sub>, and R<sup>6A</sup>, if present, is —H, or R<sup>6</sup> and R<sup>6A</sup> together form a substituted N-oxide free radical selected from substituted pyrrolidinyloxy N-oxide free radical, substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

22. (Withdrawn) Use according to claim 10 wherein R<sup>7</sup> is —ONO<sub>2</sub> or a substituted N-oxide free radical selected from substituted pyrrolidinyloxy N-oxide free radical,

substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

23. (Withdrawn) Use according to claim 10 wherein said N-oxide free radical is selected from the substituted 5- or 6- member rings of general formulae 3a and 3b



wherein X is  $-\text{CH}_2-$ ,  $-\text{O}-$  or  $-\text{S}-$ ;

Z is  $-\text{CH}_2-$  or  $-\text{CH}_2\text{-CH}_2-$ ;

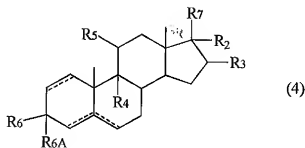
$\text{R}^1$  is  $-\text{H}$ ,  $-\text{OH}$ ,  $-\text{OCOCH}_2\text{-PEG}$ , linear or branched  $\text{C}_1\text{-C}_5$  alkyl, linear or branched  $\text{C}_1\text{-C}_5$  alkyl substituted by  $-\text{ONO}$ ,  $-\text{ONO}_2$ ,  $-\text{SNO}$ , or  $-\text{NONOate}$  or  $-\text{OC(O)R}^{15}$ , wherein  $\text{R}^{15}$  is  $\text{C}_1\text{-C}_5$  alkyl, or 5- or 6-member heteroaryl; and  $\text{R}^9$  and  $\text{R}^{10}$  are independently, linear or branched  $\text{C}_1\text{-C}_5$  alkyl groups, or substituted linear or branched  $\text{C}_1\text{-C}_5$  alkyl groups, wherein said alkyl group may be independently substituted by  $-\text{ONO}$ ,  $-\text{ONO}_2$ ,  $-\text{SNO}$ ,  $-\text{NONOate}$  or  $-\text{OC(O)R}^{14}$ , wherein  $\text{R}^{14}$  is  $\text{C}_1\text{-C}_5$  alkyl, or 5- or 6-member heteroaryl.

24. (Withdrawn) A multifunctional steroid compound comprising
- i) a steroid component,
  - ii) at least one SOD mimic component, and
  - iii) at least one NO donor component,
- for use as a medicament.

25. (Withdrawn) A multifunctional steroid compound according to claim 24, wherein said steroid component is selected from corticosteroids, estrogens, progesterones, androgens, analogs thereof, and derivatives thereof.
26. (Withdrawn) A method of treating or preventing a disorder selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, Chronic Obstructive Pulmonary Diseases (COPDs), bronchial hyperreactivity, respiratory distress syndrome or Chronic Obstructive Airway Disease (COADs), allergic conditions, arthritis, autoimmune hematologic disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-versus-host disease, multiple sclerosis, Alzheimer diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, disorders related to learning, disorders related to olfaction, disorders related to nociception, cerebral edema, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions, drug and disease-induced neuropathies and nephropathies, pathological uterine contractions, sinus tachycardia, ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders, hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholesterolemia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion tissue injury, chemotaxis and phagocytic impairment in immunological disorders, aging-mediated changes, cerebrovascular diseases, thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection, in a mammal in need thereof comprising administering to said mammal an effective amount of a multifunctional steroid compound comprising
- i) a steroid component,

- ii) at least one SOD mimic component, and optionally
- iii) at least one NO donor component.

27. (Withdrawn) A method according to claim 26, wherein said administration or treatment is selected from the group consisting of topical, oral, and parenteral.
28. (Withdrawn) A method according to claim 26, wherein said administration or treatment is selected from the group consisting of suppository, by way of injection, and by way of infusion.
29. (Withdrawn) A method according to claim 26, wherein said multifunctional steroid compound is administered by a route selected from intramuscular, intraperitoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, implant, inhalation spray, nasal, vaginal, rectal, sublingual, and urethral.
30. (Withdrawn) A method according to claim 26, wherein said mammal is human.
31. (Currently amended) A multifunctional steroid compound of formula (4)



optical isomers thereof, ~~salts thereof,~~ and ~~solvates~~ salts thereof;

wherein ----- is a single or double bond, with the proviso that two double bonds are not adjacent;

R<sup>2</sup> is NO donor, —H, or —OH, —CH<sub>3</sub>, —OC(O)R<sup>8</sup> wherein R<sup>8</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl or 5- or 6-member heteroaryl, or R<sup>2</sup> and R<sup>7</sup> together form a substituted N-oxide-free radical;

$R^3$  is  $-H$ ,  $-OH$ , or  $-CH_3$ ; or  $R^2$  and  $R^3$  together form a heterocyclic ring;

$R^4$  is  $-H$  or halogen;

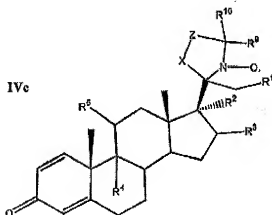
$R^5$  is  $-H$ ,  $-O$ ,  $NO$  donor or a substituted N-oxide free radical;

$R^6$  and  $R^{6A}$  are  $-O$ ,  $NO$  donor, and

$R^{6A}$ , if present, is  $-H$ , or  $R^6$  and  $R^{6A}$  together form a substituted N-oxide free radical; and

$R^7$  is  $-H$ ,  $NO$  donor, or a substituted N-oxide free radical wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring, which ring is optionally substituted by  $-OCOCH_2-PEG$  wherein said PEG may be optionally coupled to another steroid compound, and which ring is further optionally substituted by one or more independently selected  $C_1-C_5$  alkyl groups which may be further independently substituted by a group selected from an NO donor component,  $-SR^{11}$ ,  $-halogen$ , and  $-OC(O)R^{13}$  wherein  $R^{11}$  is  $C_1-C_5$  alkyl and wherein  $R^{13}$  is  $C_1-C_5$  alkyl or 5- or 6-member heteroaryl, or  $R^2$  and  $R^7$  together form a substituted N-oxide free radical; and

wherein the nitrogen of the N-oxide group in the substituted N-oxide free radical is within a 5- or 6- member ring substituted by one or more independently selected  $C_1-C_5$  alkyl groups which may be further independently substituted by an NO donor component; and wherein said NO donor is a group comprising one of  $-ONO_2$ ,  $-ONO$ ,  $-SNO$ , and  $-NONOate$ ; and with the proviso that said compound contains at least one N-oxide free radical and at least one NO donor wherein said multifunctional compound has structure IVc



in which

R<sup>1</sup> is —H or —ONO<sub>2</sub>;

R<sup>9</sup> and R<sup>10</sup> are independently linear or branched C<sub>1</sub>-C<sub>3</sub> alkyl groups;

X is —CH<sub>2</sub>—, —O— or —S—; and

Z is —CH<sub>2</sub>— or —CH<sub>2</sub>-CH<sub>2</sub>—.

32. (Canceled)

33. (Canceled)

34. (Canceled)

35. (Canceled)

36. (Canceled)

37. (Canceled)

38. (Canceled)

39. (Canceled)

40. (Currently amended) A compound according to claim 31 wherein R<sup>3</sup> is —H, —OH, or —CH<sub>3</sub>; R<sup>4</sup> is —H, F, or Cl; and R<sup>5</sup> is —H, —O, or —ONO<sub>2</sub>.

41. (Currently amended) A compound according to claim 31 wherein X is —CH<sub>2</sub>— or —O—, Z is —CH<sub>2</sub>—, and R<sup>9</sup> and R<sup>10</sup> are independently methyl or ethyl.

42. (Currently amended) A compound according to claim 31 wherein R<sup>2</sup> and R<sup>5</sup> are is —H or —ONO<sub>2</sub>.

43. (Canceled)

44. (Currently amended) A compound according to claim 31 wherein R<sup>7</sup> is —ONO<sub>2</sub> or a substituted N-oxide free radical selected from substituted pyrrolidinyloxy N-oxide free radical, substituted piperidinyloxy N-oxide free radical, substituted oxazolidinyloxy N-oxide free radical, substituted oxazinyloxy N-oxide free radical, substituted thiazolidinyloxy N-oxide free radical and substituted thiazinyloxy N-oxide free radical.

45. (Canceled)

46. (Original) A pharmaceutical composition comprising a compound according to claim 31.

47. (Original) A pharmaceutical composition according to claim 46, further comprising a component selected from carrier, binding agent, stabilizer, adjuvant, diluent, excipient, surfactant, odorant, and second pharmaceutically active agent.

48. (Original) A pharmaceutical composition according to claim 46, for use as a medicament in treating and preventing a disorder selected from the group consisting of asthma, chronic bronchitis, bronchiectasis, bronchospasms, emphysema, pneumonia, Chronic Obstructive Pulmonary Diseases (COPDs), bronchial hyperreactivity, respiratory distress syndrome or Chronic Obstructive Airway Disease (COADs), allergic conditions, arthritis, autoimmune hematologic disorders, systemic lupus erythematosus, systemic dermatomyositis, thrombocytopenia, psoriasis, contact dermatitis, atopic dermatitis, exfoliative dermatitis, acne, hirsutism, erythema nodosum, inflamed cysts, discoid lupus, bullous diseases, collagen vascular diseases, malignancies, neoplastic disease, trauma, shock, acute and chronic inflammatory conditions, sarcoidosis, Sweet's disease, graft-versus-host disease, multiple sclerosis, Alzheimer diseases, Parkinson's diseases, amyotrophic lateral sclerosis, convulsive disorders, AIDS-dementia, disorders related to learning, disorders related to olfaction, disorders related to nociception, cerebral edema, migraine, ophthalmic disorders, chronic adrenal insufficiency, congenital adrenal hyperplasia, gastrointestinal diseases, hepatic diseases, inflammatory bowel disease, Crohn's disease, ulcerative colitis, renal disease, gastric secretory and peristaltic functions, drug and disease-induced neuropathies and nephropathies, pathological uterine contractions, sinus tachycardia, ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, atherosclerosis, rheumatic disorders, hypertension, arrhythmia, hyperthyroidism, cellular defense impairment, hypercholestermia, Reaven's Syndrome, vasculitis, arteritis, endothelial dysfunction-induced diseases, diabetes mellitus, insulin-resistance and glucose intolerance in diabetes, ischemia-reperfusion

tissue injury, chemotaxis and phagocytic impairment in immunological disorders, aging-mediated changes, cerebrovascular diseases, thyrotoxicosis, aggregation disorders, fertility conditions and reproductive disorders, menopause, ovarian dysfunction, testicular dysfunction, and penile erection.

49. (Withdrawn) A kit for administration of a multifunctional steroid compound comprising i) a dosage amount of at least one multifunctional steroid compound that comprises a steroid component, at least one SOD mimic component, and optionally at least one NO donor component;

ii) instructions for use; and

iii) optionally means for the delivery of said compound.

50. (Withdrawn) A kit according to claim 49 comprising one of items selected from inhaler, spray dispenser, syringe, or suppositories.